

In the specification:

Please amend the specification as shown below:

Please replace the paragraph on page 1, lines 10-23 with the following:

Genetic manipulation of the yeast genome provides a convenient model for identifying essential genes required for eukaryotic cell replication, growth, and death. The complete DNA sequence of the yeast *Saccharomyces cerevisiae* strain S288C was determined through an international collaboration of more than 100 laboratories on April 1996. General information and databases containing the yeast genome of about 6000 genes are available publicly and can be found for example on public websites such as for example: <http://www.ncbi.nlm.nih.gov/Yeast>; ~~<http://genome-www.stanford.edu/Saccharomyces/>~~. Other databases exist as well and these databases and links therein to other websites are equally suitable for the purposes of this invention. The examples include but are not limited to Yeast GenBank (A collection of all GenBank sequences that are derived from *Saccharomyces cerevisiae*); Yeast Swiss-Prot (The collection of Swiss-Prot protein sequences that are derived from *Saccharomyces cerevisiae*); YPD (The Yeast Protein Database maintained by Proteome, Inc.), and periodic updates thereof the content of which is incorporated herein by way of reference. Methods of manipulating yeast are well established and are well known to those skilled in the art and can be found in publicly available web sites by using appropriate keywords, e.g., yeast and protocol, among many others.

Please replace the paragraph on page 2, lines 9-18 with the following:

In the past this task was accomplished on a case by case basis, whereby investigators used known gene manipulation techniques and screening methods and applied such methods or techniques to each specific gene of interest or to each particular gene combination. Yeast is often selected as a model due to the ease of manipulation and possibility of screening a large number of candidates in a relatively short period of time. Yeast have the highest rate of recombination

and gene conversion among organisms tested, which is several orders of magnitude higher than in mammals. In the post-genomic era, serial gene-knockout programs in yeast (which you can tell by tetrad analysis, e.g.,

<http://bioinformatics.weizmann.ac.il/pub/software/mac/mactetrad69.readme>) confirm that about 1 in 6 gene products are essential to the life of that cell (their deletion is lethal) under tested conditions. While a reasonable fraction of tested gene products are enzymes, other genes have either unknown function or their function does not fit into apriori postulation.

Please replace the paragraph bridging page 19, line 18 to page 20, line 17 with the following:

This invention provides yeast mutants as models of cancer and other diseases associated with deregulation of cell growth and replication. Yeast is an extremely useful model of studying human diseases. For Example, as of January 20, 1996 the following human diseases and clinically important conditions have been identified as having matches between human genes and *S. cerevisiae* genes/proteins: Hereditary Non-polyposis Colon Cancer; Cystic Fibrosis; Wilson Disease; Glyceral Kinase Deficiency; Adrenoleukodystrophy; Ataxia Telangiectasia; Amyotrophic Lateral Sclerosis; Myotonic Dystrophy; Lowe Syndrome; Neurofibromatosis, Type 1; Choroideremia; Diastrophic Dysplasia; Lissencephaly; Thomsen Disease; Wilms Tumor; Achondroplasia; Menkes Syndrome; Multiple Endocrine Neoplasia 2A; Wiskott-Aldrich Syndrome; Duchenne Muscular Dystrophy; Aniridia; Gonadal Dysgenesis; Breast and Ovarian Cancer, Early Onset; Chronic Granulomatous Disease; Epidermolytic Palmoplantar Keratoderma; Waardenburg Syndrome; Adenomatous Polyposis Coli; Neurofibromatosis, Type 2; Kallmann Syndrome; Tuberous Sclerosis; Polycystic Kidney Disease; Aarskog-Scott Syndrome; Marfan Syndrome; Huntington Disease; Spinocerebellar Ataxia; Long QT Syndrome, Type 1; Fragile X Syndrome; Emery-Dreifuss Muscular Dystrophy; Retinoblastoma; McLeod Syndrome; Norrie Disease; Von Hippel-Lindau Disease; Alzheimer Disease; Hyperekplexia; Agammaglobulinemia, X-linked (for detailed information see <http://www.ncbi.nlm.nih.gov/Basnett/Yeast/> and updates thereof as incorporated herein by way of reference). Means of cross-referencing the yeast and human genes are now achievable and can be for example performed using "XREF2" program as found on <http://www.ncbi.nlm.nih.gov/XREFdb/>, which is incorporated herein by way of reference.

Abnormalities in components of the cell cycle surveillance system have been identified in human cancers and other diseases such as listed above. These abnormalities include alterations in cyclin (80-90% of tumors), p53 (50-60% of tumors), and DNA mismatch repair (10-20% of some tumor types such as colon and pancreatic). Often the primary genetic alteration is a loss of function and so a drug discovery program focused on these defects would require restoring the lost function. An alternative approach is to identify which other protein(s) when inhibited selectively kill cells that have the primary defect.

Please replace the paragraph bridging page 20, line 18 to page 21, line 8 with the following:

General information and databases containing yeast genome are available publicly and can be found for example on public websites such as for example: <http://bioinformatics.weizmann.ac.il>; <http://ourworld.compuserve.com/homepages/CVelten/yeast.htm>; <http://www.ncbi.nlm.nih.gov/Yeast>; <http://genome-www.stanford.edu/Saccharomyces/>; [genome-ftp.stanford.edu \(directory/yeast/genome_seq\)](http://genome-ftp.stanford.edu/directory/yeast/genome_seq); <http://vectordb.ateg.com/vectordb/>; <http://www.mpimg-berlin-dahlem.mpg.de/-andy/GN/S.cerevisiae/>; or <http://www.mips.biochem.mpg.de/proj/yeast>, the content of which and links therein are incorporated herein by way of reference. Other databases exist as well and these databases and links therein to other websites are equally suitable for the purposes of this invention. The examples include but are not limited to Yeast GenBank (A collection of all GenBank sequences that are derived from *Saccharomyces cerevisiae*); Yeast Swiss-Prot (The collection of Swiss-Prot protein sequences that are derived from *Saccharomyces cerevisiae*); YPD (The Yeast Protein Database maintained by Proteome, Inc.), and periodic updates thereof the content of which is incorporated herein by way of reference. Methods of manipulating yeast are well established and are well known to those skilled in the art and can be found in publicly available web sites such as for example www.goshen.edu/bio/yeast, www.fhere.org/~gottschling, and www.saes.ucsf.edu/home/HerskowitzLab, among many others.